REMARKS

Applicant requests that the amendment of April 25, 2007 not be entered. Claim 1 has been further amended in light of a telephone interview held with Examiner Blanco on June 7, 2007 to discuss the rejection to claim 1 under 35 USC §102(b) in view of Takazawa *et al.*, Meijs *et al.* and Chudzik *et al.*

Interview With Examiner Janier Blanco

As an initial point, Applicant's agent sincerely appreciates and thanks Examiner Blanco for his assistance and time afforded from his schedule to discuss the instant application with the objective of advancing it to allowance.

At the suggestion of the Examiner, and at the further proposal of the Applicant, claim 1 has been amended to further specify in the preamble that the corneal implant is "for improving or correcting vision".

Claim 1 has also been amended for greater clarity and to better define the scope of protection sought by the Applicant. The wording of the claim makes it clear that the membrane formed from a solution of a biological polymer mixed with a polyacrylamide is dried **and then hydrated** for use as a corneal implant. Support for claim 1, as amended, may be found throughout the description, for example, at: page 13, lines 21 to 23; page 16, lines 22 to 29 (Example 1); page 17, lines 23 to 31 (Example 3); page 18, lines 12 to 13 and 17 to 29 (Example 4); page 19, lines 8 to 10 (Example 5) and lines 16 to 18 and 22 to 23 (Example 6); and page 20, lines 11 to 13.

Applicant respectfully submits that neither Takezawa *et al.*, Meijs *et al.* nor Chudzik *et al.* disclose or teach a corneal implant for **improving or correcting vision** comprising a membrane made from a polymer solution that has been dried to form a membrane and the membrane has been **hydrated** for use as a corneal implant.

ARGUMENTS

There are now 22 claims pending.

Claims 11 and 32 have been amended to correct minor grammatical errors.

Claims 27 and 28 have been withdrawn.

Claim 29 has been amended to depend on claim 1.

Claims 31 and 33 have been amended to include "proteins" among the list of bioactive compounds. Support for the amendment may be found in the description, for example, at page 13, lines 21 to 23, page 14, lines 3 to 8 and page 20, lines 10 to 13.

New claims 34 and 35 have been added which are directed to preferred embodiments of the invention that are supported by the specification as originally filed, for example, at:

Claim Number	Support
34	Page 6, lines 16 to 23; Example 7, Table II
35	Page 14, lines 15 to 20; Example 1

No new subject matter has been added.

Election/Restriction

The Examiner indicates that the decision regarding the restriction requirement/election of the claims of Group I (i.e now claims 1 to 5, 8 to 15, 25, 26 and 29 to 33) has been made final. Accordingly, claims 27 and 28 of Group II have been withdrawn from consideration as the non-elected group, along with claims 6 and 7.

35 USC §112, 1ST Paragraph – Claims 30 and 31

The Examiner has rejected claims 30 and 31 alleging that the claimed subject matter has not been adequately described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor was in possession of the claimed subject matter. More specifically, the Examiner alleges that the specification does not support a

hydration solution comprising "a drug, a bioactive compound or combination thereof". Applicant respectfully disagrees.

Support for the subject matter of claims 30 and 31 may be found explicitly throughout the description, for example, at:

Page 13, lines 21 to 22	The physical properties of the membrane may be modified for example as a function of rehydration, or via the presence of lipids and/or proteins. [Emphasis added.]
Page 14, lines 3 to 10	The membrane of the invention may further comprise/have associated with it various compounds e.g. drugs, biological materials (e.g. peptides/proteins, lipids, etc.), crosslinkers, plasticizers, cytokines, etc. to fulfill or further contribute to an aspect of the desired functionality of the corneal implant in any particular situation. Such agents or compounds may be introduced during the making of the membranes or after their formation. [Emphasis added.]
Page 19, Example 5	A variety of agents or compounds (e.g., crosslinking, plasticizer, drugs, cytokines) can be introduced during the making of the membranes from examples I to IV. Compounds can be introduced either during the mixing of both collagen and pNIPAAm or after the formation of a membrane. The latter can be dried, thereby, the agents can be introduced during the rehydration process. Otherwise, the agents can be introduced on the rehydrated membrane. [Emphasis added.]
Page 20, lines 11 to 13	Albumax (a lipid rich bovine serum albumin, ...) can be added during rehydration with Hank's balanced salt solution (HBSS). [Emphasis added.]
Table I, last entry	Albumax (2x)

The specification teaches that the dried membrane can not only be hydrated with pure water or any salt buffered solution, but also with a solution containing one or more soluble compounds such as proteins/peptides, growth factors, cytokines or drugs (e.g., antibiotics, antiviral agents, agonists, antagonists). The hydration process is performed prior to implantation so that the adsorbed or trapped compound can eventually be released into the cornea defect or the diseased cornea. Adsorption of proteins/peptides and other soluble compounds is a well-recognized phenomenon in the field of implant research.

Applicant therefore submits that claims 30 and 31 satisfy the written description requirement so that a skilled person would reasonably conclude that the inventor had possession of the claimed subject matter at the time the application was filed.

Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

35 USC §102(b)

Claims 1 to 4, 8 to 10 and 29 to 33 have been rejected for lack of novelty in view of Takezawa *et al.*

Claims 1, 2, 4, 10, 25, 26 and 30 to 33 have also been rejected as anticipated in view of Meijs *et al.* and **claims 1, 4, 10, 15, 25, 26 and 30 to 33** have been rejected as anticipated in view of Chudzik *et al.*

Claim 1 has been amended as follows:

> A corneal implant for improving or correcting vision comprising a ~~hydrated~~ membrane, said ~~hydrated~~ membrane ~~comprising a mixture~~ formed from a solution of a biological polymer ~~and~~ mixed with a polyacrylamide, wherein said solution has been dried to form a membrane and the membrane has been hydrated for use as a corneal implant.

Claim 29 has been amended to depend on claim 1 and therefore, is no longer an independent claim. Claims 2 to 4, 8 to 10, 15, 25, 26 and 30 to 33 are amended by virtue of their dependency, either directly or indirectly, to claim 1, as presently amended.

Applicant respectfully submits that claim 1, and dependent claims thereon, are novel and patentably distinguishable over the prior art.

MPEP §2131 provides that:

> "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described in a single prior art reference." *Verdegaal Bros. V. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The **identical invention**

must be shown in as complete detail as contained in the ... claim." [Emphasis added.] *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). The elements must be arranged as required by the claim.

MPEP §2121.01 also provides that:

> "In determining that quantum of prior art disclosure which is necessary to declare an applicant's invention 'not novel' or 'anticipated' within section 102, the stated test is whether a reference contains an **'enabling disclosure'** (...)." *In re Hoeksema*, 399 F.2d 269, 158 USPQ 596 (CCPA 1968). [Emphasis added.].

Takezawa *et al.*

Takezawa *et al.* describe a cell culture substrate comprising collagen and pNIPAAm to support human dermal fibroblast cells. The purpose of their research was to make a polymer substrate of spheroids in cell culture so that the polymer property can be changed as a function of temperature (LCST). The advantage is that the cell sheet and/or clusters grown on the polymer substrate can be removed by changing the temperature of the substrate. When the temperature of the polymer substrate is reduced below the LCST, there is a transition from the gel-like state to a dry, more dense state which involves a conformational, or shape, change in the polymer molecules. This conformational or physical change in the polymer molecules permits the cells to be detached without the use of proteolytic enzymes such as trypsin which is known to destroy bonds between neighbouring cells and compromise cell function.

Applicant respectfully submits that the claimed invention is novel and patentably distinguishable over Takezawa *et al.* for a number of reasons.

As an initial point, the application of the polymer composition described in the Takezawa reference is for use as a cell culture substrate. The utility is completely different from, and irrelevant to, an application for use as a corneal implant as defined in claim 1 for improving or correcting vision. Although the membrane of the corneal implant promotes

cell in-growth and epithelialization, both the membrane and the cells remain permanently attached to each other following insertion of the implant into a subject. In other words, the membrane is **not** intended for use as a **temporary** substrate for the cultivation, proliferation and subsequent detachment of corneal cells following insertion of the implant. Alternatively, the corneal implant is intended to be used a permanent device for corneal repair and/or transplantation and for improving and correcting vision.

In every example described throughout the Takezawa *et al.* reference, their cell culture substrate is used to anchor and adhere human dermal fibroblast cells and not **corneal epithelial cells** which are intrinsic to the natural tendency or purpose of the subject matter defined in claim 1.

Furthermore, the Takezawa reference does not disclose or teach a corneal implant comprising a membrane made from a polymer solution that has been dried to form a membrane and the membrane has been **hydrated** for use as a corneal implant. Throughout the instant specification it is taught that the mixed polymer solution is dried to form a membrane and that the membrane is hydrated for use as a corneal implant. Drying of the mixed polymer solution produces an interpenetrating hydrogel network which strengthens and stabilizes the formed membrane **without any chemical bonds** (see, for example, page 11, line 31 to page 12, line 1). **Hydration** of the dried membrane alters its physical properties centrally required for functionality (e.g. optical clarity), pliability (e.g. easy for the surgeon to manipulate/handle) and wearability (e.g. wettable) as a corneal implant. Furthermore, the hydration step allows the membrane to be **removed** from the mold once it has been dried (see, for example, page 17, lines 29 to 31).

With respect to hydration of the membrane, the Examiner argues:

> Takezawa *et al.* disclose a hydrated (throughout the mixture of chemical compounds, there is at least one step of hydration; in addition, see page 11, lines 15-20) membrane/substrate ... .

Applicant disagrees with the Examiner's assessment of the prior art. The passage to which the Examiner refers to at page 11, lines 15 to 20 describes a cell detachment

process using trypsin/EDTA. This is **not** a hydration step but rather the addition of proteolytic enzyme to show that cells detached from the cell culture substrate do not form a cell sheet using the prior art process. There is absolutely no teaching or suggestion in the Takezawa reference or examples in making the polymer substrate (i.e. Examples 1 and 2) that specifically describes hydration of the polymer substrate after it is formed and before cell cultivation. Furthermore, because the example referred to by the Examiner describes **how to use** the polymer substrate to culture and detach cells using a solution of trypsin/EDTA, a skilled person would not interpret this process as being the same as hydrating a dried membrane as described in the instant application. Accordingly, the Examiner's argument that adding trypsin/EDTA to a polymer substrate with attached cell clusters/sheets anticipates claim 1 is misplaced. As described throughout the instant application, the hydration step of the membrane of the instant invention occurs after the membrane has been dried and before it used as a corneal implant; not after implantation of the membrane and corneal cell in-growth and epithelialization.

Meijs *et al.*

Meijs *et al.* describe a cell growth material and corneal implant using telechelic perfluorinated polyether polymers having a functionalized or polymerized group. The cell growth substrate polymer is comprised of a polymerizable macromonomer having the formula:

$$Q\text{-}(PFPF\text{-}L)_n\text{-}1\text{-}PFPF\text{-}Q$$

wherein PFPF is a perfluorinated polyether $-OCH_2CF_2O(CF_2CF_2O)_x(CF_2O)_yCF_2CH_2O-$, L is a difunctional linking group and Q is a polymerizable group.

The cell growth substrate may also be formed from a copolymer using the polymerizable macromonomer having the formula shown above and a hydrophilic comonomer such as, for example, acrylamide. The reference further describes that the cell growth polymer substrate may additionally includes adsorbed or coupled glycoproteins to the polymer substrate surface to promote cell adhesion.

Applicant respectfully submits that the claimed invention is also novel and patentably distinguishable over Meijs *et al.*

Firstly, Meijs *et al.* describe using **telechelic perfluorinated polyether polymer** (i.e. a synthetic polymer) having the formula described above. In contrast, the instant invention uses **polyacrylamide**. The Examiner alleges that Meijs *et al.* describe a corneal implant formed from a polymer of an acrylamide and refers to column 7, line 49 to column 8, line 33 of the reference. Applicant disagrees with the Examiner because this section describes **copolymer** formed from telechelic perfluorinated polyether comonomer **and** acrylamide comononer. A copolymer of telechelic perfluorinated polyether and acrylamide is **not** the same as a polyacrylamide. By definition a copolymer is a polymer consisting of **two** or more different monomers. On the other hand, a polymer is a naturally occurring or synthetic compound consisting of large molecules made up of a linked series of repeated simple monomers

Secondly, Meijs *et al.* do not describe a corneal implant comprising a membrane formed from a solution of a biological polymer **mixed** with a polyacrylamide. In contrast, this reference describes using adhesive glycoproteins (biological polymer) that are **adsorbed** or **coupled** to the polymer substrate surface. Adsorption is defined as a process in which a molecule is overlaid on a substrate and remains in place; coupling is connecting two ends together of adjacent molecules. The Meijs reference also describes polymers **coated** with collagen (see examples 11 to 14) which is not the same as **mixing** a solution of a biological polymer with a polyacrylamide as recited in claim 1.

Chudzik *et al.*

Chudzik *et al.* describe a crosslinkable macromer system for use as a crosslink matrix between a tissue site (i.e. host tissue) and an implant or prosthetic device, i.e. as an interface or "grout", to permit tissue growth through the crosslink matrix and between the tissue site and implant. The macromer comprises a polymeric backbone to which are covalently bonded two or more polymer-pendent polymerizable groups and one or more polymer-pendent initiator groups. The polymeric backbone can be a polyamino acid (e.g. collagen) (see column 6, line 64 to column 7, line 3) and the pendent polymerizable

group can be an acrylamide (see column 6, lines 58 to 63). The polymerizable groups are incorporated into the macromer using standard thermochemical reactions. An example of a reaction resulting in collagen-containing pendent polymerizable moieties is described at column 9, lines 1 to 7. The initiator group has the important characteristic of being able to be coupled to a preformed macromer containing polymerizable group, or to be modified to form a monomer which can take part in the macromer synthesis followed by the addition of polymerizable groups. A long list of examples of initiators is given at column 6, lines 43 to 52.

Applicant respectfully submits that the claimed invention is also novel and patentably distinguishable over Chudzik *et al.*

Chudzik *et al.* do not describe a **corneal implant** for improving or correcting vision comprising a membrane formed from a solution of a biological polymer mixed with a polyacrylamide as defined in claim 1. In contrast, the prior art reference describes an intermediate material for use as an **interface** between host tissue and an implant/device to promote a variety of biological responses towards the device. Furthermore, the corneal implant of the instant invention comprises a membrane produced **only** by **mixing** a biological polymer, such as collagen, with polyacrylamide. Drying of the mixed polymer solution produces an interpenetrating hydrogel network which strengthens and stabilizes the formed membrane without any chemical bonds (see, for example, page 11, line 31 to page 12, line 1). There is no bulk polymerization or other chemical reaction involved in combining a solution of the two polymers which is dried to form a membrane. The biological polymer and polyacrylamide used in producing the corneal implant are also in the form of **inert** polymers and therefore, do not have any polymerizable groups, nor any initiator groups incorporated into a polymer backbone, e.g. the biological polymer is also not **polymerizable collagen** as described at column 23, Example 19. The corneal implant of the instant invention is fabricated from biocompatible materials which avoids the use of harsh chemical reactions (as described in the prior art) that can impair cell viability through cytotoxicity effects and thus, hinder cell growth and healing when implanted in a subject.

In view of the above comments, Applicant asserts that claim 1, and all dependent claims therefrom, are clearly novel and patentable distinguishable over Takazawa *et al.*, Meijs *et al.* and Chudzik *et al.*

Accordingly, reconsideration and withdrawal of the rejections are respectfully requested.

35 USC §103(a)

The Examiner has rejected certain of the claims as obvious having regard to Meijs *et al.* individually (i.e. claims 15 and 29), or in combination with one or the other of Perez *et al.* (i.e. claims 5, 13 and 14), Graham *et al.* (i.e. claims 11 and 12) and Takezawa *et al.* (i.e. claims 2 and 3). Applicant disagrees that the claims are obvious in view of the prior art references.

As discussed *supra* (see (102(b) rejection), claim 1, and dependent claims 2, 3, 5, 11 to 15 and 29 thereon, have been amended to specify that the corneal implant for improving or correcting vision comprises a membrane that is formed from a solution of a biological polymer mixed with a polyacrylamide that is dried to form a membrane and the dried membrane is hydrated.

Meijs *et al.* and Takezawa *et al.*

The Meijs *et al.* and Takezawa *et al.* references are discussed *supra* (see 102(b) rejection).

Perez *et al.*

Perez *et al.* describe a **two-layer** composite material composed of a hydrogel and a thin layer of corneal tissue or collagen matrix. The hydrogel is formed from an **electron-beam crosslinkable polymer** that is directly **covalently attached** to the collagen matrix, or an intermediate material is used to adhere the hydrogel and the collagen matrix together.

Graham *et al.*

Graham *et al.* also describe a **two-layer** corneal implant comprising a lens body and a porous core having an outer surface made of a hydrogel composition containing water and a hydrophilic polymeric material. A **coating** of a synthetic polymeric material is located on the outer surface of the core and **covalently bonded** to the hydrogel composition.

Claims 2, 3, 5, 11 to 15 and 29 are Inventive Over The Prior Art

As an initial point, and as stated in Applicant's previous response, Takezawa *et al.* relates to a non-analogous field of scientific endeavour and therefore, can not be used individually, or in combination with any other reference, to establish a *prima facie* case of obviousness. A person interested in fabricating an artificial corneal implant for improving or correcting vision would not look for guidance in the field of cell culture substrates.

Applicant further submits that the Examiner's rejection of claims 2, 3, 5, 11 to 15 and 29 for obviousness is improper because the Examiner has repeatedly focused on individual elements or features of the claimed invention without showing how the claimed invention, **as a whole**, is suggested by the prior art (as is required by the applicable authorities). It is well established under U.S. patent law and practice that focusing on individual elements of the claimed invention, rather than on the invention as a whole, is not the proper test under 35 U.S.C. §103. In ascertaining the differences between the prior art and the claims at issue, it is essential to view the claims as "the invention as a whole". In so doing, it is improper to focus on the obviousness of substitutions and differences between the claimed invention and the prior art rather than on the obviousness of the claimed invention as a whole relative to that prior art.

Furthermore, because an invention is assessed based on a combination of features, consideration must be given to whether or not the state of the art was such as to suggest to a skilled person precisely the combination of features claimed. The Examiner has not explained or articulated explicit or factual findings as to how the prior art would have

suggested to a skilled person to make changes to any of the references necessary to arrive at Applicant's invention that would support a 35 U.S.C. §103 rejection. The fact that an individual feature or a number of features were known does not conclusively show the obviousness of a combination. The question not whether the skilled person with access to the entire prior art, could have made the combination according to the invention, but whether he actually would have been motivated to do so in expectation of an improvement.

On this point, the Court stated in *Environmental Designs v. Union Oil Co. of Cal.* (713 F.2d 693, 698 (Fed. Cir. 1983)):

> All the pieces of the present invention were known in the art, i.e., the equations for hydrogenation and hydrolysis of sulfur compounds, the simultaneity of chemical reaction, and the components of the Claus effluent. That all elements of an invention may have been old (the normal situation), or some old or some new, or all new, is however, simply irrelevant. Virtually all inventions are combinations and virtually all are combinations of old elements. A court must consider what the prior art as a whole would have suggested to one skilled in the art, *In re McLaughlin*, 443 F. 2d 1392, 1395, 170 U.S.P.Q. 209, 212 (1971).

The court in *Connell v. Sears, Roebuck & Co.*, 722 F.2d 1542, 1549 (Fed. Cir. 1983), also stated:

> The opinion says obviousness is established when features that "distinguish" the invention from the closest reference are disclosed in analogous structures in which the features perform an identical function. It is not "features" but the subject matter of the invention "as a whole" that must be considered, 35 U.S.C. §103. That features, even distinguishing features, are "disclosed" in the prior art is alone insufficient. As above indicated, it is common to find elements or features somewhere in the prior art. Moreover, most if not all elements perform their ordained and expected function. The test is whether the claimed invention as a whole,

in light of all the teachings of the references in their entireties, would have been obvious to one of ordinary skill in the art at the time the invention was made. 35 U.S.C. § 103.

Accordingly, Applicant submits that the instant invention is inventive and patentably distinguishable over the prior art and that the Examiner has not established a *prima facie* case of obviousness based on the cited prior art references.

Reconsideration and withdrawal of the rejections are respectfully requested.

In view of the foregoing, early favourable consideration of this application is earnestly solicited. It is believed this responds to all of the Examiner's concerns, however if the Examiner has any further questions, Elizabeth A. Hayes-Quebec (Reg. No. 48,305) may be contacted at 613-232-2486. Further, if the Examiner does not consider that the application is in a form for allowance, an interview with the Examiner is requested.

Respectfully submitted,

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